REMARKS

Reconsideration of this application, is respectfully requested. Claims 1, 11, 12, 14, 15, 18-22 have been amended. Claims 16 and 17 have been cancelled. New claims 23-28 have been inserted. With these amendments, claims 1, 4-15, and 18-26 are currently pending in this application. These amendments are made without prejudice or disclaimer and do not add any new matter. Applicants retain the right to prosecute any cancelled or otherwise unclaimed subject matter in a continuing, divisional or other application as appropriate. Consideration and entry of this reply is respectfully requested.

Amendments to the Specification

The specification has been amended to insert a sequence listing. The undersigned hereby declares that the content of the paper and computer readable copies of the Sequence Listing are identical in content. The sequence listing contains no new matter as all of the sequences contained in the sequence listing are found in the application as originally filed (e.g., paragraph [0085]).

The specification has been amended to incorporate the language of originally filed claims 18-21 into the Detailed Description (para. 45). The amendment does not constitute new matter as the subject matter was originally filed in original claims 18-21. Applicants believe this amendment is proper and entry thereof is respectfully requested.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 8-10 and 14-17 stand rejected under 35 U.S.C. § 112, second paragraph as to the limitations: i) "the cytokine" (claims 8-10); (ii) "the cytokine is a T cell activating cytokine" (claim 14); and, (iii) "the T cell activating cytokine" (claims 15-17). The Examiner alleges there is insufficient antecedent basis for these terms following the previous amendment of claim 1. Claims 8-10 and 16 have been cancelled; the rejection as to these claims is therefore moot. Claims 14, 15 and 17 have been amended such that the objected to terms are no longer found within the claims.

Rejection Under 35 U.S.C. § 112, First Paragraph (New Matter)

Claims 1 and 4-22 stand rejected under 35 U.S.C. § 112, first paragraph, as containing new matter. This rejection was based in large part on Applicants' use of the phrase "a therapeutically effective amount of interferon". The currently amended claims no longer include this phrase; the rejection is therefore moot.

Although the amendments render the rejection moot, Applicants believe a discussion of the "toxicity" aspects of the claimed method would expedite prosecution. The Examiner indicated that "the disclosed doses of IFN-α2b appear to be problematic...because more than 1/3 of the patients tested exhibited an unintended toxic effect, rather than a therapeutic effect." Applicants respectfully disagree with the Examiner's interpretation of the data. As described in the specification, the initial dose may be followed by reduced dosages if certain side effects are observed. Treatment with high doses of cytokines is known by those of skill in the art to have side effects. As described at paragraph [0083] of the instant application, patients were initially dosed with 20 MU and subsequent doses were reduced if toxicity (as defined by the National Cancer Institute, see Table 2) was observed. As shown in Table 2, none of the patients reached Grade 4 toxicity, which would require stopping treatment. Grade 3 toxicities of "constitutional symptoms" (e.g., flu-like symptoms", see para. [0091]), "elevated liver function", "granulocytopenia / luekopenia", and "neurologic toxicity" were observed in one patient per category. The majority of toxicities were Grade 2. As stated in the legend to Table 2, "[n]o patient had a third treatment interruption that would also have required removal from treatment." These side effects are typical, as explained in paragraph [0091]:

> Patients developed typical toxicities associated with HDI including flu-like symptoms, cytopenias, and liver function test abnormalities, which lasted only during the time of HDI (Table 2)...All 7 patients completed the course of HDI and no evidence of disease progression was noted. In fact, even two patients (M166 and M335) developed marked disease reduction after HDI....

Thus, the Examiner's allegations that the disclosed doses are "problematic" and exhibited an unintended toxic effect, rather than a therapeutic effect" are incorrect in view of the data presented in the specification and what is known by those of skill in the art.

Rejection Under 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 1 and 4-22 stand rejected under 35 U.S.C. § 112, first paragraph as being non-enabling. At page 8 of the Office Action, the Examiner alleges that the specification is not enabled for: 1) any antigen other than a melanoma-associated antigen; 2) "subsequent administration of any interferon other than interferon α"; or, 3) administration of interferon α2b at any dose for any regimen. Applicants respectfully disagree and traverse these rejections as indicated below.

Claim 1, part (a) was amended to define the tumor antigen as a melanoma-associated tumor antigen. Dependent claims 11 and 12 were also amended to list only melanoma-associated tumor antigens. New claims 23-26 relate to the melanoma-associated tumor antigen gp100. The first allegation in the Examiner's rejection is therefore moot.

Regarding the second and third allegations, it is first noted that claim 1, part (b), was amended to delete the phrase "a therapeutically effective amount of interferon" and limit the type of interferon to "interferon alpha". The claims therefore do not encompass any type of interferon, but only a very limited subset thereof. The Examiner alleged that no dosage regimen other than that disclosed in the Examples is enabled (subsequent administration of "any interferon other than interferon-α2b is not enabled because the specification only discloses administration of interferon-α2b and the status of art at the time of filing indicated the unpredictabilities in the efficacy of adjuvant interferon therapy of melanoma"). The Examiner refers to the Sabel et al. reference, the FDA's "approval of high-dose interferon-alpha-2b for the post-surgical therapy of high-risk melanoma", and "[c]oncerns regarding the design and interpretation of the clinical trials, the cost and toxicity of treatment, and the appropriate selection of patients who should be treated...." In light of such "unpredictabilities", the Examiner states that "only the dose regimen disclosed in the specification of instant application is considered enabled." Applicants respectfully disagree as indicated below.

The enablement requirement is satisfied if, given what those of skill in the art already know, the specification teaches enough that they can make and use the invention without "undue experimentation." Genentech v. Novo Nordisk, A/S, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed.Cir.1997); In re Vaeck, 947 F.2d 488, 495. It is well-

established that "a patentee need not test all the embodiments of his invention" so long as "he provide[s] a disclosure sufficient to enable one skilled in the art to carry out the invention commensurate with the scope of his claims." Amgen v. Chugai and Genetics Institute, 927 F.2d 1200, 1213 (Fed. Cir. 1991). Applicants do not believe this to be a case in which the claims are so broad, the results so unpredictable, and the examples so limited that there is not an adequate basis of support for the amended claims. In re Soll, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938).

As previously discussed and acknowledged by the Examiner, the specification describes at, for example, Examples 1 and 2 (see, in particular, paragraph [0083]), that therapeutically effective amounts of IFN-α2b were found to range from 20 to six megaunits (MU) (the dosing being adjusted downward from an initial 20 MU depending upon the toxicity observed in each patient). A key attribute of the claimed method is that the initial administration of a high dose of IFN-α stimulates the patient's immune response against the melanoma-associated tumor antigen to which that patient was previously immunized. Applicants' believe it is reasonable to expect the skilled artisan to be able to select an appropriate dose from within the claimed range. An undue burden would not be placed on the skilled artisan to select an initial dose of IFN-α of between, for example, approximately 10 and the currently accepted highest dose allowed by the FDA (e.g., 20 MU for IFN-α2b as noted by the Examiner. The range of the intial dose is neither unlimited nor outside of reason. Similarly, the skilled artisan would not be unduly burdened in selecting a particular type of IFN-α (see, for example, para. [0045] of the instant specification). There are only a limited number of IFN-α species that may be selected; choosing from among these would not subject the skilled artisan to an undue amount of experimentation. Applicants believe the claims are enabled to the extent required under the law (see the above-described legal precedents of Genentech, Vaeck, Amgen, and Soll). Accordingly, withdrawal of these rejections is respectfully requested.

CONCLUSIONS

Reconsideration of this application is respectfully requested. Applicants believe the claims are in condition for allowance and respectfully request the issuance of a Notice of Allowance as soon as possible. The Examiner is encouraged to contact the undersigned if it is believe doing so would expedite prosecution of this application.

Respectfully submitted,

Date: July 3, 2008

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